

Target Advancement

PROGRAM GOAL

Part of our annual *Edmond J. Safra Core Programs for PD Research*, the Target Advancement program seeks to build conclusive evidence to rationalize biological pathways and targets for Parkinson's disease (PD) therapeutic development. Funding will support projects focused on validating PD relevant targets implicated primarily in disease modification, but may also support targets relevant to symptomatic strategies (motor and non-motor symptoms of PD), and/or to alleviating drug-induced adverse events such as L-DOPA induced dyskinesia.

DEADLINES

Fall 2015 Review Cycle

- Informational Conference Call: March 25, 2015 at 12pm US ET
- Pre-Proposals Due: May 27, 2015 – 6pm US ET
- Full Proposal Invitations: by June 24, 2015
- Full Proposals Due (by invite only): August 5, 2015 – 6pm US ET
- Anticipated Award Announcement: October 2015
- Anticipated Funding: November 2015

Spring 2016 Review Cycle

- Informational Conference Call: August 19, 2015 at 12pm US ET
- Pre-Proposals Due: October 28, 2015 – 6pm US ET
- Full Proposal Invitations: by November 25, 2015
- Full Proposals Due (by invite only): January 13, 2016 – 6pm US ET
- Anticipated Award Announcement: March 2016
- Anticipated Funding: April 2016

*MJFF will hold a 45-minute conference call on the dates and times listed above to clarify and explain the goals of this funding initiative and answer applicant questions. To participate in the call and receive call-in details, please RSVP to conferencecalls@michaeljfox.org.

BACKGROUND AND RATIONALE

Research into the etiology, pathophysiology and therapy of PD is providing unprecedented information on biological mechanisms underlying the disease and its treatment. MJFF is intent on leveraging and translating basic research rapidly to promote novel therapeutic development by pharmaceutical and biotech companies. To this end, MJFF believes that promoting critical target validation studies within academic and industry laboratories can help de-risk investments in therapeutic development and ultimately accelerate the creation of innovative therapies for PD patients.

PURPOSE

MJFF evaluates PD relevant targets against several criteria before investing in therapeutic development programs and considers a target sufficiently validated when each of the following target characteristics are replicated and cross-validated across research entities:

- Genetic link or differential tissue expression in PD patients
- Ability to modulate the target *in vivo* using genetic or pharmacological manipulations to yield successful therapeutic outcomes in multiple *whole* mammalian PD models

MJFF has supported many studies focused on identifying and manipulating PD relevant targets and biological pathways through its previous Target Validation Program. In 2015, the program is being expanded and renamed the Target Advancement program with the goal of promoting work through three modified funding opportunities:

- Target Validation Pilot Awards: One-year grants to support research on characterizing promising novel PD-relevant targets.
- Target Optimization Awards: Two-year grants supporting collaborative teams to validate targets within MJFF-defined priority biological pathways. The selection of the pathway will change each funding cycle based on MJFF internal assessment of the field.
- Priority Target Awards: One-year grants supporting target biology work on a high-priority MJFF target.

PROGRAM REQUIREMENTS

Proposed research for all three Target Advancement award programs should focus on filling key translational gaps (see MJFF validation requirements above) specific to a particular target. Preference will be given to proposals utilizing experimental systems with high construct and predictive validity to human PD such as patient-derived material and/or animal models utilizing clinically translatable endpoints. Types of studies that can be proposed include:

- Demonstrating PD therapeutic relevance of the target or neural substrate by determining the consequences of manipulating its activity/expression in relevant animal models
- Post-mortem tissue expression studies to determine target distribution patterns in normal and pathological states
- Elucidation of target biology in relevant *in vitro*, cellular and *in vivo* models to understand physiological and pathological roles of the target as well as the potential for safety liability
Projects that utilize human-derived tissues where appropriate are encouraged
- Development of animal model or tool
- Identifying up-stream or downstream signaling nodes that may be therapeutically targeted

Target Validation Pilot Awards

Target Validation Pilot Awards are well-suited to projects where hypothetical or experimental rationale is compelling for a target's role in PD and study results can make the case for continuing (or discontinuing) a line of research. Priority will be given to proposals for targets that can already demonstrate one or more of the following:

- Genetic association of the target or its pathway to PD etiology, pathophysiology, symptoms or treatment response
- Altered expression or function of the target or its pathway in PD-relevant human tissue
- Clinical trial data implicating the target, target pathway, or neural substrate in PD

Target Optimization Awards

Funding will utilize a collaborative model to support teams to develop and execute systematic, milestone-driven studies of targets within an MJFF-nominated priority pathway. Teams will seek to significantly enhance data supporting or refuting the validation of targets within the defined pathway through use of complementary experimental strategies. Applicants are encouraged to conduct independent replication and cross-validation studies and teams are required to be composed of multi-institutional collaborators.

PD is characterized neuropathologically by build-up of protein aggregates and research has shown protein folding and clearance mechanisms to be implicated in protein aggregate formation and accumulation. As such, for the Fall 2015 funding cycle, MJFF has identified the protein handling pathway as a priority for further target validation.

Applicant teams may submit proposals to validate any target within this pathway; however, priority will be given to targets with relevant human target validation data (see above) and at least one published positive target validation study in a whole *mammalian* animal model of PD. Examples of targets that MJFF has identified that meet these criteria include:

- LAMP-2A
- NEDD-4
- TFEB
- VPS35

Collaborative grants are goal-oriented, milestone-driven project plans focused on answering a major research question in the PD field. As such, investigators will interact regularly with MJFF staff and its advisors to discuss study design, research directions, progress against milestones, and troubleshooting solutions.

Priority Target Award

The Priority Target Award is well-suited to projects focusing on filling key gaps in priority target understanding and manipulation within the context of disease and treatment biology. Applicants may submit proposals on any of the following MJFF prioritized targets:

- Alpha-synuclein
- GBA
- LRRK2
- Parkin
- Trophic factors

MJFF has made significant investments in the above high-priority targets. Applicants may submit proposals to this funding opportunity if the proposed work meets the criteria of the program, however, consideration of these proposals will be case-by-case and carefully evaluated against the existing MJFF portfolio in these areas.

FUNDS AVAILABLE

Target Validation Pilot Awards support one-year grants up to \$100,000 total costs inclusive of both direct and indirect costs. No more than 10% of the direct costs may go to indirect costs. Target Optimization Awards support two-year grants up to \$400,000 total costs inclusive of both direct and indirect costs. No more than 25% (academic institutions) or 10% (for-profit organizations) of the direct costs may go to indirect costs.

Priority Target Awards support one-year grants up to \$100,000 total costs inclusive of both direct and indirect costs. No more than 10% of the direct costs may go to indirect costs.

Please see the program instructions, Administrative Guidelines, and our FAQ on MJFF indirect cost policy for additional details.

ELIGIBILITY REQUIREMENTS

Applications may be submitted by:

- U.S. and non-U.S. biotechnology/pharmaceutical companies or other for-profit entities, either publicly or privately held.
- U.S. and non-U.S. entities, public and private non-profit entities, such as universities, colleges, hospitals, laboratories, units of state and local governments, and eligible agencies of the federal government.
- Post-doctoral fellows are eligible to apply as Principal Investigator (PI) to the Target Validation Pilot Awards program only and must collaborate with an Administrative PI who directs the laboratory in which the fellow will conduct research. The Administrative PI will be responsible for assisting in providing all institutional documents required for the project and will be required to sign any award contract. Training or mentoring-only proposals will not be considered.

ADMINISTRATIVE GUIDELINES

Please refer to our [Administrative Guidelines](#). Please note that any information contained in the above program description and additional program instructions will supersede any information contained in general MJFF administrative guidelines.